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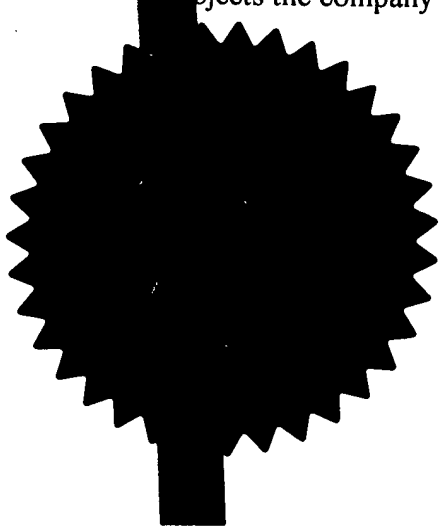

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04JUN99 E451923-6 002806
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1.	Your reference	AHT0003
2.	Patent application number *(The Patent Office will fill in this part)*	9912908.2
3.	Full name, address and postcode of the or of each applicant *(underline all surnames)*	OPTISCAN LIMITED, OLD HORSE YARD, COMBERTON ROAD, TOFT, CAMBRIDGE, CB3 7RY.
	Patents ADP number *(if you know it)*	
	If the applicant is a corporate body, give the country/state of its incorporation	UNITED KINGDOM 7659732001
4.	Title of the invention	METHOD OF AND APPARATUS FOR DETERMINING SKIN HISTOLOGY
5.	Name of your agent *(if you have one)*	~~Barker Brettell~~ Beresford & Co
	"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	~~138 Hagley Road Edgbaston Birmingham B16 9PW~~ 16 High Holborn London WC1 6BX
	Patents ADP number *(if you know it)*	~~7442494002~~ 1826001

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		Country	Priority application number *(if you know it)*	Date of Filing *(day/month/year)*
6.	If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number			

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7.	If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application		

8.	Is a statement of inventorship and of right to grant of a patent required in support of this request *(Answer 'Yes' if:* *a) any applicant named in part 3 is not an inventor, or* *b) there is an inventor who is not named as an applicant, or* *c) any named applicant is a corporate body.* *See note (d))*	YES

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Continuation sheets of this form	
Description	20 + 20
Claim(s)	
Abstract	
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Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature Barker Brettell Date

Barker Brettell 03 June 1999

12. Name and daytime telephone number of person to contact in the United Kingdom

Mr. A.H. Tebbit Tel: 0121 456 1364

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METHOD OF AND APPARATUS FOR DETERMINING SKIN HISTOLOGY

The present invention relates to a method of and apparatus for the non-invasive determination of skin histology and it is particularly, but not exclusively, concerned with a method of and apparatus for identifying and measuring the presence, depth and concentration of chromophores within the skin. The presence and extent of chromophores within the skin is considered to be an important indicator of a variety of ailments and other conditions. The invention is considered to be potentially useful for the preliminary screening of patients to identify those who should be referred to an appropriate clinician for diagnosis and further to assist the clinician in diagnosis and in some embodiments to indicate whether a given treatment would be of value to the patient.

In order to appreciate the presence of abnormalities in the skin it is first necessary to have an appreciation of the structure of normal skin.

The skin is divided into two main layers, the epidermis and the dermis, each of which is itself divided into several sub-layers. Starting from the deepest layer, the subcutaneous layer is overlain by a reticular layer of the dermis which is composed of course and dense interlacing collagen fibres which are intermingled with reticular fibres and elastic fibres. Over this is the papillary dermal layer which is also composed of collagen fibres but these are much finer than those of the reticular layer. The dermis is also rich in blood vessels. Above the papillary dermis is the dermo-epidermal junction, where lies the germinative layer of the epidermis. It is in the germinative layer that epithelium cells multiply continuously to replace cells lost from the surface of the epidermis. The germinative layer also contains melanocytes for the production of melanin. The epithelium cells

from the germinative layer move upwards into the layer above which is called the spinous layer, and thence into the granular layer where the cells contain granules which are involved in the formation of keratin. It is in this granular layer that the cells of the epidermis die. Above the granular layer, is a clear and translucent layer and above that is the outermost layer the cornified layer. This is composed of clear dead scale-like skin which is progressively lost from the surface by exfoliation.

In normal healthy circumstances, the epidermis is translucent and transmits light diffusely; a proportion of incident light will be absorbed in the epidermis, depending in part on the amount of melanin present in the epidermis, and a proportion will be transmitted through to the dermis. Because the papillary dermis largely consists of a very fine network of collagen fibres (as low as 2μm in diameter), light passing through the papillary dermis will be subject to Rayleigh scattering. A proportion will be scattered inwards and a proportion will be back-scattered, and some light will be remitted back through the epidermis. In the reticular dermis the fibres are bundled together and largely parallel to the skin surface: thus they are too coarse to be subject to Rayleigh scattering, and light penetrating to the reticular dermis will continue until absorbed or deflected by some discontinuity.

Thus light remitted by the epidermis will have its spectral characteristics altered by the effects of melanin, blood and other chromophores in the skin.

We have previously noted (see WO 98/22023) that the thickness of the papillary dermis can vary quite considerably, and that this will have a marked effect on the skin colour, but that it is possible to construct a mathematical model which allows corrections to be made for this effect.

When so corrected it is notable that the colour of normal healthy human skin lies in a well defined surface area within a particular colour space, for example the CIE LMS colour space. That surface area encompasses all colours of normal healthy human skin irrespective of the amount of melanin within the skin and thus irrespective of race or degree of tanning. This approach allows a more accurate and repeatable approach to measuring parameters and chromophores regarding the skin through optical means than previously existing techniques.

The present invention relates to apparatus for and methods of monitoring light remitted from human skin or images thereof.

According to the present invention, there is provided apparatus for monitoring the presence of one or more chromophores in skin, which apparatus comprises

a light source for projecting light to illuminate an area of skin,

a photo-receptor for receiving light re-emitted by the illuminated area of skin, and spectroscopic analyser means for monitoring the remitted light

a comparator having means for comparing variations in the intensity and spectral characteristics of the re-emitted light with respect to the intensity and spectral characteristics of the projected light at different wavelengths and with a record of the intensity and spectral characteristics of light remitted by normal healthy skin and means for emitting a control signal in response to any such variations.

The invention extends to a method of monitoring the presence of one or more chromophores in skin, which method comprises

illuminating an area of skin by projecting light from a light source,

receiving light re-emitted by the illuminated area of skin at a photo-receptor, and spectroscopically analysing the remitted light.

Such a method advantageously includes the steps of feeding signals corresponding to such variations to a comparator and comparing variations in the intensity and spectral characteristics of the re-emitted light with respect to the intensity and spectral characteristics of the projected light at different wavelengths and with a record of the intensity and spectral characteristics of light remitted by normal healthy skin, and emitting a control signal in response to any such variations.

The apparatus and method of the present invention may be utilised for monitoring the presence of a wide variety of chromophores in the skin. It is possible to derive data relating to the presence, depth, and concentration of a wide range of chromophores, depending on measurements being made at particular wavelengths. These wavelengths may readily be selectable by light filters which may be substituted into the light path, or the analyser may be constituted by a spectroscope. The filters may be broad band filters or narrow band filters as appropriate for the analysis to be undertaken.

Examples of particular chromophores whose presence may be monitored include: melanin, blood, haemoglobin, oxy-haemoglobin, bilirubin, tattoo pigments, keratin, collagen and hair.

The control signal may be used for controlling or operating one or more of the following: a display device such as a display monitor, a printer, or a medical laser or other treatment device or apparatus.

The projected light is preferably polarised, and the remitted light is suitably cross-polarised before monitoring. This is especially suitable for monitoring the presence of chromophores beneath the epidermis. Since little scattering of light takes place in the epidermis, any cross-polarised light which is detected must have been remitted from or via the (papillary)

dermis, and this allows surface effects and the effects of the epidermis to be eliminated. A similar effect can be achieved without using cross-polarised illumination by coating the surface of the skin with a transparent oil which removes direct reflections at the skin surface.

A method and apparatus according to the invention are valuable in providing information to a clinician on which the clinician may base a diagnosis or a course of treatment and the apparatus may be used for controlling the treatment and in some cases for giving an indication of whether the treatment may be effective or not.

For example, so-called port-wine stains may be diagnosed by straight-forward visual inspection, and it is well known to treat them by laser to cauterise the blood vessels supplying that blood. Typically treatment for such a problem begins with the firing of a series of "test shots" by a laser at different powers to establish the minimum power necessary to cauterise the blood vessels. That power will depend on the depth and the size of those vessels, and these may vary over the extent of the lesion. The test powers are chosen by the clinician having regard to his skill and past experience. This technique suffers from a number of disadvantages. It is not very reliable since the depth and the size of the blood vessels may vary over the extent of the lesion. It is time consuming since the results of the test need to be assessed after a healing time. And the patient is left in a state of uncertainty during that time. This uncertainty is exacerbated due to the fact that a too intense laser irradiation will result in burning of the skin and consequent permanent scarring. In the cases of up to about one third of patients, the intensity of irradiation which would be required to cauterise the offending blood vessels is actually so high that there would be a serious risk of scarring and the treatment is accordingly contra-indicated.

The present invention can be used to establish not only the amount of blood present, and thus give an indication of the amount of blood vessels required to be cauterised, but also the depth of those vessels beneath the surface of the skin. The intensity of laser irradiation needed to cauterise a given amount of blood vessels is known from past experience or can be established, and the absorption characteristics of human skin in relation to the laser radiation of a given wavelength can readily be established (indeed handbooks supplied with medical lasers tend to contain this information).

Thus by making use of the present invention, light remitted from the stain can be analysed to give an indication of the melanin content of the epidermis (which governs its absorption coefficient) and of the depth and concentration of the offending blood vessels, and a prediction can be made there and then as to the intensity of laser irradiation which will be required to effect a satisfactory treatment and whether that intensity would give an acceptably low risk of permanent scarring. Further this assessment may be made at as many points over the extent of the stain as are thought necessary. Not only that, but the output signal from the apparatus may be used to control firing of a laser. Thus the power output of the laser may be varied as it is directed over the extent of the lesion. Thus the laser may be controlled to give the minimum effective power dissipation over the various increments of the lesion. Parts only of the area of the lesion could be treated if that would give a cosmetically acceptable result. And if the lesion was so severe that it was unsuitable for laser treatment, the patient could be told immediately and would not face some weeks of uncertainty.

Similar considerations apply in the case of removing tattoos by the destruction of the pigments used to make them, and the removal of moles by the destruction of melanin by which they are constituted.

The removal of hair by laser cauterisation of the hair bulb may also be controlled by apparatus according to the invention. Hair consists of keratin and its colour (and thus light energy absorption characteristics) is due to the presence of melanin. The hair bulb is located in or below the reticular dermis. Using the present invention it is possible to determine the absorption characteristics of the skin layers which would have to be penetrated by laser radiation aimed to destroy the hair bulb. The absorption characteristics of the hair bulb can be measured or calculated from a measurement of the melanin content of the hair, and the amount of energy which would have to be absorbed by the hair bulb to destroy it can also be determined, in vitro if necessary. From this information, it is possible to calculate the energy which would require to be dissipated by the laser, and it would accordingly be possible either to give a minimum energy dosage, or to predict that the minimum required dosage was so high that permanent scarring would result and that the treatment should accordingly not be carried out.

It will be appreciated that the output signal generated by the use of the invention will represent an average value over the extent of the area monitored: this will plainly be no greater than the size of the light spot which is illuminated, and its size may also be determined by the size of the photoreceptor. Means may be provided for varying the monitored area if desired, for example from a spot 0.1 mm or less to 10 cm or more in diameter. This can be extended to provide an image of an area by providing the analysis at a number of locations. This can easily be achieved by the use of a digital camera.

To achieve these results, the system measures the light remitted from skin and compares it with the incident light at a number of wavelengths or wavelength bands. These measurements can be performed using any

convenient means including filters or a spectrometer and they allow quantification of the quantities and position, including distance relative to the dermo-epidermal junction, of chromophores such as collagen, melanin, blood and keratin. Indeed these measurements can be performed on any substance assuming its absorbency and reflectivity of light are known. "Spectral measurement" is used to denote measurement of the light remitted from human skin whether by the use of a spectrometer or sub-sampling through filters which can be placed in the path of the incident or remitted light. The spectral measurements can be performed at one or more points. A collection of points whether gathered simultaneously or not can also be combined to form an image showing the measurements over the skin.

The spectral remittance of light from human skin can be calculated given knowledge of the quantity and position of substances within it. Such calculations can be performed using a variety of mathematical means including monte carlo modelling and the Kublenka-Munk theory, generating a value for P_n where

$P_n(\rho_1, \rho_2, \rho_3 \ldots \rho_n, d_1, d_2, d_3 \ldots d_n, \phi_{m1}, \phi_{m2}, \phi_{m3} \ldots \phi_{mn}, d_m, \nu, \kappa) =$ *Equation 1*

$$\frac{\int_0^\infty R(\rho_1,\rho_2,\rho_3 \ldots \rho_n, d_1, d_2, d_3 \ldots d_n, \phi_{m1}, \phi_{m2}, \phi_{m3} \ldots \phi_{mn}, \nu)\theta(\lambda, d_m, \kappa)^2 S(\lambda) S_{P_n}(\lambda) d\lambda}{\int_0^\infty S(\lambda) S_{P_n}(\lambda) d\lambda}$$

in which:

P_n represents the calculated or measured ratio of remitted to incident light for a particular wavelength function or filter $S_{P_n}(\lambda)$ and incident light $S(\lambda)$. θ represents the light absorbed within the epidermis with d_m representing the quantity of epidermal melanin and κ the amount of keratin. R represents the ratio of light remitted from the dermis to light incident on the dermis, with $\rho_1, \rho_2, \rho_3 \ldots \rho_n$ representing the quantity of blood within n layers within the dermis, parallel with the skin surface and

of thicknesses $d_1, d_2, d_3 \ldots d_n$. Within these layers, $\phi_{m1}, \phi_{m2}, \phi_{m3} \ldots \phi_{mn}$ represent the quantity of melanin within the dermis and ν the thickness of the papillary dermis. P_n can also be obtained through measurements on real skin rather than by calculation.

As discussed the position within the dermis and concentration of blood is of importance to the calibration and use of medical lasers. The position of such blood will effect the remitted light from the skin generally causing the skin colour to become more purple as the depth of blood vessels increases.

To ascertain non invasive information regarding blood position and concentration the spectral composition of light remitted from skin can be ascertained as above for a representative sample of possible blood quantities and blood depths. It is also necessary to generate the possible set of remitted light measurements relating to variations in other parameters such as epidermal melanin, dermal melanin, papillary dermal thickness and keratin. As such an N dimensional search space is generated where N corresponds to the number of different constituents and blood and melanin planes considered. This analysis can be extended to include any other constituents such as tattoo pigment. For analysis of skin this may have to include spectral measurements within the infrared portion of the electromagnetic spectrum as well as the visible.

Measurements of the spectral remittance from skin to be examined are then compared with the data within the N dimensional search space with the closest match indicating the constituents of the skin. The data for these comparisons can either be performed as required or incorporated into pre calculated lookup tables.

Such an analysis may require a large search and it is possible for certain combinations of constituents to generate the same spectral remittance and thus multiple solutions.

Another approach is to identify those constituents of skin about which information can reliably be ascertained, quantify these and perform a transformation to the measured spectral remittance or data to which this is to be compared.

This can for instance be achieved by first adjusting for variations in the thickness of the papillary dermis in the manner described in International Patent Application published as WO 98/22023. A second quantity that must also be assessed is the quantity of melanin within the epidermis. The accuracy to which this can be assessed has a large influence on the accuracy to which the depth of blood within the dermis can be ascertained. However the presence of blood at different depths within the dermis markedly changes the remittance of light from the skin and so complicates the assessment of epidermal melanin levels by standard spectroscopic means.

A solution to this problem assumes that the quantity of epidermal melanin does not change markedly over the skin surrounding the lesion thus allowing interpolation from the surrounding areas. Such a technique may operate in certain lesions but the reliance that can be placed on the results will be lowered. A second solution is to assess the levels of epidermal melanin by a spectroscopic/light analysis method accepting any inaccuracies due to the complicating factor of blood at different depths. Following either of these techniques the N dimensional space can be reduced requiring only solutions to P_{nr} to be found where

$$P_{nr}(\rho_1,\rho_2,\rho_3,d_1,d_2,d_3)=\int_0^{\infty}R_{nr}(\rho_1,\rho_2,\rho_3,d_1,d_2,d_3)S(\lambda)S_{P_n}(\lambda)d\lambda \quad \textit{Equation 2}$$

As discussed inaccuracies in this measurement will adversely effect the assessment of blood position within the dermis thus lowering its accuracy.

A third solution is to use a detector which is "blind" to the effect of melanin within the epidermis. Such a detector would register zero, or a constant value, when presented with melanin within the epidermis with differences in its value corresponding purely to the quantity and position of other skin constituents. Such a detector would not require transformations to data based on measures for the amount of epidermal melanin thus increasing accuracy. It is also possible to use such a detector in the generation of the N dimensional search space discussed previously.

The epidermal-melanin-blind detector renders the pigment melanin effectively transparent when it lies within the epidermis of the skin. Such a detector allows viewing of structures within the skin with the obscuring effect of epidermal melanin removed. The approach outlined utilizes knowledge of the variation of light absorption by melanin within the epidermis with wavelength.

At a particular wavelength λ, let the ratio of remitted to incident light from skin be $P(\lambda)$. If two wavelengths λ_1 and λ_2 are considered this leads to two values of P, $P(\lambda_1)$ and $P(\lambda_2)$.

Let $R_d(\lambda,\upsilon)$ represent the ratio of remitted to incident light from bloodless, melanin-free, normal dermis with a known quantity of collagen within the papillary dermis υ. Further let $\theta(\lambda,d_m)$ represent the ratio of incident to transmitted light for melanin where d_m represents the quantity

of melanin. As shown in the International Patent Application published as WO 98/22023, $P(\lambda)=\theta(\lambda,d_m)^2 R_d(\lambda,\upsilon)$ and therefore

$$P(\lambda_1)=\theta(\lambda_1,d_m)^2 R_d(\lambda_1,\upsilon) \qquad \textit{Equation 3}$$

and

$$P(\lambda_2)=\theta(\lambda_2,d_m)^2 R_d(\lambda_2,\upsilon). \qquad \textit{Equation 4}$$

As further shown in *"The optics of human skin"* The Journal of Investigative Dermatology, (R. Anderson, B. Parrish & J. Parrish), $\theta(\lambda,d_m)$ can represented in the form $\theta(\lambda,d_m)=e^{-d_m m(\lambda)}$ *Equation 5*

where $m(\lambda)$ is the spectral absorption coefficient of melanin. As such Equations 3 and 4 become

$$P(\lambda_1)=e^{-2d_m m(\lambda_1)}R_d(\lambda_1,\upsilon) \qquad \textit{Equation 6}$$

and

$$P(\lambda_2)=e^{-2d_m m(\lambda_2)}R_d(\lambda_2,\upsilon) \qquad \textit{Equation 7}$$

By taking the natural logarithm of both sides of equations 6 and 7 can be shown to equate to

$$\ln P(\lambda_1)=\ln e^{-2d_m m(\lambda_1)}+\ln R_d(\lambda_1,\upsilon) \qquad \textit{Equation 8}$$

and

$$\ln P(\lambda_2)=\ln e^{-2d_m m(\lambda_2)}+\ln R_d(\lambda_2,\upsilon) \qquad \textit{Equation 9}$$

which can be simplified to

$$-2d_m m(\lambda_1)=\ln P(\lambda_1)-\ln R_d(\lambda_1,\upsilon)=V_1 \qquad \textit{Equation 10}$$

and

$$-2d_m m(\lambda_2)=\ln P(\lambda_2)-\ln R_d(\lambda_2,\upsilon)=V_2 \qquad \textit{Equation 11}$$

The proposition for an epidermal blind detector is that $V_1-CV_2=0$ where C is a constant. For this to be true

$$-2d_m m(\lambda_1)+2Cd_m m(\lambda_2)=0 \qquad \textit{Equation 12}$$

and therefore

$$C=\frac{m(\lambda_1)}{m(\lambda_2)} \qquad \textit{Equation 13}$$

leading to

$$\ln P(\lambda_1) - \ln R_d(\lambda_1,\upsilon) - C(\ln P(\lambda_2) - \ln R_d(\lambda_2,\upsilon)) = 0 \quad \textit{Equation 14}$$

This discussion assumes bloodless skin where the only melanin present exists in the epidermis. For real skin however this will often not be the case, with blood, melanin in the dermis and keratin etc. being present. In this situation an extra term $E(\lambda)$ is introduced to the right hand side of equations 8 and 9 representing the extra absorption, or indeed reflectance, introduced through the additional constituents leading to

$$\ln P(\lambda_1) = \ln e^{-2d_m m(\lambda_1)} + \ln R_d(\lambda_1,\upsilon) + \ln E(\lambda_1) \quad \textit{Equation 15}$$

and

$$\ln P(\lambda_2) = \ln e^{-2d_m m(\lambda_2)} + \ln R_d(\lambda_2,\upsilon) + \ln E(\lambda_2) \quad \textit{Equation 16}$$

and therefore

$$\ln P(\lambda_1) - \ln R_d(\lambda_1,\upsilon) - C(\ln P(\lambda_2) - \ln R_d(\lambda_2,\upsilon)) = \ln E(\lambda_1) - C\ln E(\lambda_2) = F \quad \textit{Eqn 17}$$

As $P(\lambda_1)$ and $P(\lambda_2)$ can be measured, C is known, and $R_d(\lambda_1,\upsilon)$ and $R_d(\lambda_2,\upsilon)$ can be calculated as disclosed in the International Patent Application published as WO 98/22023, F can thus be calculated. The value of F therefore indicates information about the extra terms $E(\lambda_1)$ and $E(\lambda_2)$ with

$$F = C\ln E(\lambda_2) - \ln E(\lambda_1) \quad \textit{Equation 18}$$

and therefore

$$e^F = \frac{E(\lambda_2)^C}{E(\lambda_1)} \quad \textit{Equation 19}$$

In summary to operate the epidermal melanin blind detector measurements P_1 and P_2, where $P_1 = P(\lambda_1)$ and $P_2 = P(\lambda_2)$, of skin are made and R_1 and R_2, where $R_1 = R_d(\lambda_1,\upsilon)$ and $R_2 = R_d(\lambda_2,\upsilon)$, are calculated. F is then calculated from $\ln P_1 - \ln R_1 - C(\ln P_2 - \ln R_2)$ with its value giving information about pigments and components other than epidermal melanin.

The above analysis is based on the use of two measurements at two separate frequencies. However this can be extended to broad band filters with values of m, the spectral absorption coefficient of melanin, calculated for each broad band filter.

As $E(\lambda)$ relates purely to the change in remitted light, whether absorbed or reflected, without reference to the quantity of epidermal melanin or papillary dermal thickness it is simple to calculate it for blood at different quantities and depths within the dermis. The measured values of $E(\lambda)$ can then be compared with these thus returning information regarding the depth of blood vessels.

This approach can be extended to analyse constituents other than blood with the removal of epidermal melanin such as the examination of keratin, tattoo pigments, dermal melanin etc. Indeed the concept of a melanin blind detector can be extended to a blood blind detector, tattoo pigment blind detector and indeed any constituent for which the light reflectance and absorbency are known.

By allowing an accurate measurement of the depth and concentration of blood vessels and other constituents, these measurements can then be used within Equation 1 thus allowing an accurate measurement of epidermal melanin.

The knowledge gained regarding the position and constituents of human skin can be utilised in Equation 1 to form a number of important measures. For instance the percentage of light at any particular wavelength, or wavelength band, which is absorbed by epidermal melanin can be ascertained. This information can then be used to calculate the likelihood of scarring occurring and thus allow the setting of a safe

maximum intensity of light, whether through a laser or other illumination device, that can be applied to the skin.

Further, the intensity, or percentage of light, passing through the entire papillary dermis can be ascertained. This is calculable using an equation similar to Equation 1 to result in the ratio, T, of incident light to light passing through the entire papillary dermis being calculated for a particular wavelength function or filter $S_{Pn}(\lambda)$ and incident light $S(\lambda)$.

$T(\rho_1, \rho_2, \rho_3 \ldots \rho_n, d_1, d_2, d_3 \ldots d_n, \phi_{m1}, \phi_{m2}, \phi_{m3} \ldots \phi_{mn}, d_m, \nu, \kappa) =$ *Equation 20*

$$\frac{\int_0^\infty T_d(\rho_1, \rho_2, \rho_3 \ldots \rho_n, d_1, d_2, d_3 \ldots d_n, \phi_{m1}, \phi_{m2}, \phi_{m3} \ldots \phi_{mn}, \nu)\theta(\lambda, d_m, \kappa)S(\lambda)S_{P_n}(\lambda)d\lambda}{\int_0^\infty S(\lambda)S_{P_n}(\lambda)d\lambda}$$

T_d represents the light transmitted through the papillary dermis and can be calculated using a variety of mathematical means including monte carlo modelling and the Kublenka-Munk theory.

Such a measure is useful in quantifying the intensity that might impinge on a hair bulb and thus can be used to judge the efficacy of hair removal by laser or other light source.

Similarly the intensity or percentage of light that reaches blood at a particular depth can be ascertained and from this the quantity absorbed by the blood. Such a measure allows an assessment or calculation of the effectiveness of the light in treating the blood vessels.

Following the quantification of the intensity of light impinging on various structures it is possible to ascertain, or quantify, the effect such an intensity will have on these structures. This may be performed through calculation or through analysis of previous treatments or through laboratory experiments. This knowledge then allows calculation, through

laboratory experiments. This knowledge then allows calculation, through Equation 1, of the expected appearance of the skin at either a particular wavelength or wavelength band following the application of such light. This information could, for instance, be used to generate colour, RGB, representations of the expected result of a treatment which would be of great use in the planning of such treatment.

In preferred embodiments of the invention, the spectral analysis is undertaken at more than one, for example at least four, distinct wavelengths or wavelength bands, and in some preferred embodiments, such analysis is undertaken over the whole spectrum. In a simple construction of apparatus, a filter wheel is placed between the source of illumination, and the area of skin under inspection is successively illuminated using light of the desired different wavelengths or wavelength bands. In that case, all that is necessary is to measure the intensity of remitted light for each wavelength (band). Alternatively, white light may be used and the remitted light measured by a spectrometer to give values at each of a plurality of narrow wavelength bands covering substantially the entire spectrum.

The use of narrow wavelength bands, whether due to filtering incident or remitted light or by use of a spectrometer, has advantages in certain circumstances. For example, it may be desired to distinguish between arterial blood and venous blood. Arterial and venous blood have slightly different spectral characteristics due to the presence or absence of oxy-haemoglobin. Both oxy-haemoglobin and haemoglobin remit light strongly in the red, and their spectral curves in fact largely overlap. However, venous blood, without oxy-haemoglobin has a spectral curve with a domed peak, whereas arterial blood, due to the presence of oxy-haemoglobin has a spectral curve with twin peaks separated by a valley. The use of two

narrow band filters, one at a wavelength corresponding to one or other of those peaks, and one at a wavelength corresponding to the valley in the oxy-haemoglobin spectrum and a comparison of the intensity of light remitted at those wavelengths can thus determine the presence or absence of oxy-haemoglobin and thus distinguish between venous and arterial blood.

The analysis of at least four different wavebands offers considerable advantages over previous proposals, and allows the system to be used for measuring a variety of different parameters which could not previously have been unambiguously derived from the information given. For example, it allows the offset of chromophores to be measured. By offset, we mean the distance between the dermo-epidermal boundary and the top of the population of chromophores. This is in addition to the concentration and depth of the chromophores. The problem was that the position of a spot within a three-dimensional CIE LMS colour space was not necessarily unique to a given set of measurements. The same position could be achieved by relative variation between two of the variables concerned. Previously, it had been necessary to make an estimate based on prior assumptions about the relationship between these variables. The analysis of a fourth or further wavelength band allows comparison with a notional colour space having four (or more) dimensions so that any position within that n-dimensional space can be attributed to a unique depth, concentration and offset of a particular chromophore.

A preferred embodiment of the invention will now be described with reference to the accompanying diagrammatic drawing.

In the drawing a light source 1 is arranged to direct a beam of light onto a filter wheel 2 which contains a number of filter elements 21 to 26 each of

which may selectively be brought into the light path. The number of filters may be as high as desired. One such filter may be removed for the direct transmission of light from the light source 1. The filters would together cover as much of the spectrum as required, for example from the infra red, through to the ultra violet. The light is passed to a bundle of optical fibres 3 through which it is transmitted to the skin *S* of the patient, or even to an appropriate photographic image of that skin, via a polarising filter 31. Remitted light is carried back through a second polarising filter 41 and a second bundle of optical fibres 4 to a photo-receptor unit 5. The use of the bundles of optical fibres adds greatly to the convenience of use of the apparatus since a relatively small unit at the end of a flexible lead may thereby be brought to the patient's skin *S*, and the physical posture of the patient during measurement is largely irrelevant. The two polarising filters 31, 41 are set so that their respective planes of polarisation are at right angles, to eliminate specularly reflected light.

The photo-receptor unit 5, which may simply measure the intensity of the remitted light where a series of filters is used as illustrated, emits a signal to a comparator 6 which may be constituted as a suitably programmed PC. The comparator may receive signals relating to the intensity of light remitted in the infra-red, red, yellow and blue regions of the spectrum. The comparator is arranged to assign a notional position in a colour space according to co-ordinates represented by these red, yellow and blue values and to note that position having regard to the infra-red value. Instead of measurements over the three primary wavebands, other filters may be provided so that the visible spectrum is split up into four or more wavebands. This establishes four or more co-ordinates, and the comparator may thus assign a notional position in a colour space having four or more dimensions. That position can be unique as representing the presence, depth, offset and concentration of any one or more of a range of

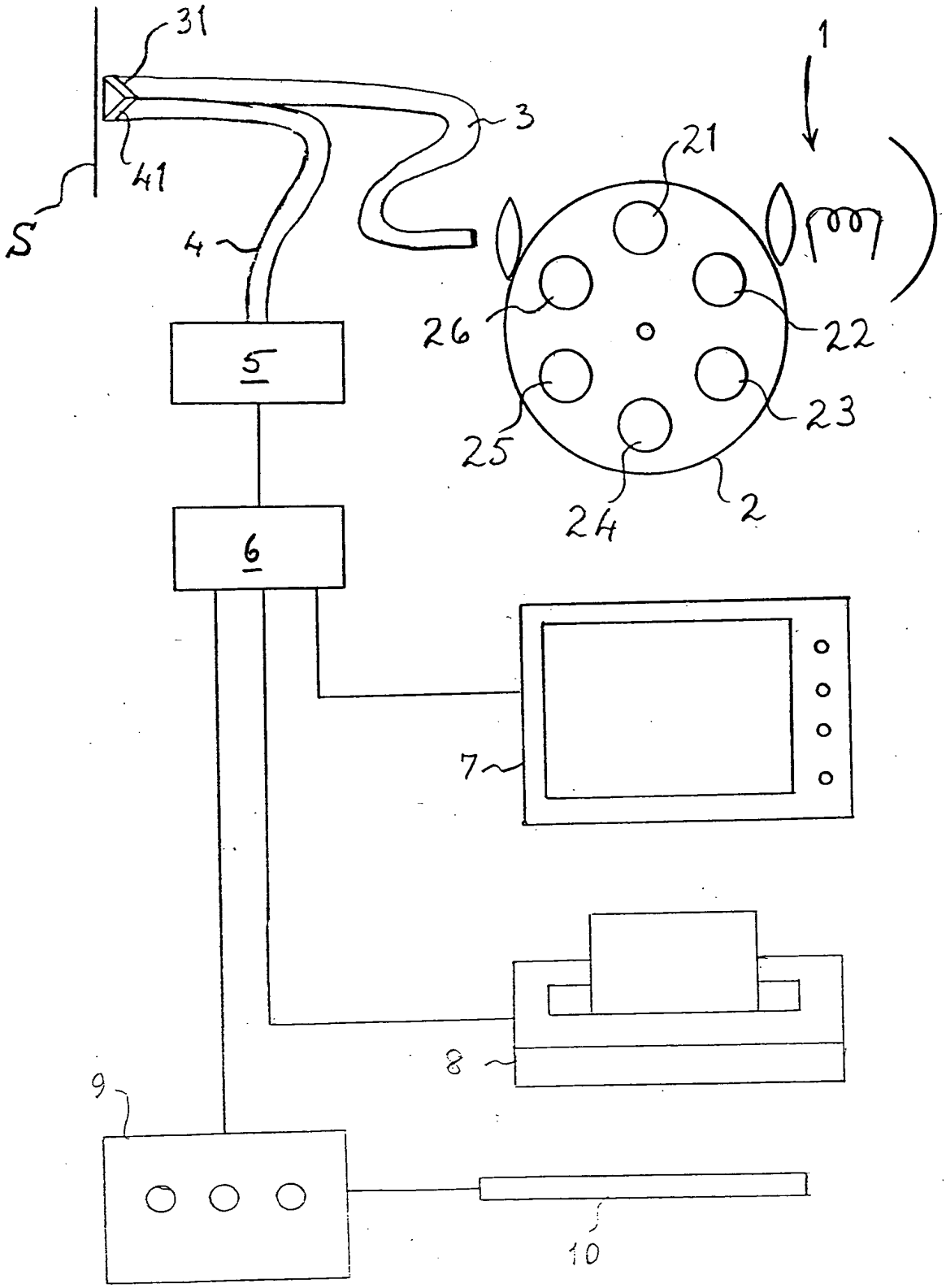
chromophores within the skin. The comparator is suitably arranged to supply the results to a display monitor 7 and/or to a printer 8, and it may be arranged to pass control signals to the power supply 9 of a medical laser 10 or other source of radiation whether coherent or non-coherent.

The present invention at least in its most preferred embodiments, enables the generation of information regarding a number of features regarding skin. To allow an accurate diagnosis of disorders of the skin, or the prognosis of treatment for such disorders, or the monitoring of healthy skin, it is important that the spatial relationship between these features can be understood. To facilitate the spatial correlation of two images, one showing the appearance of the skin and the other showing a particular feature or of two images showing different features, we have developed a technique whereby a third image is generated. Thus we also provide a method of and apparatus for showing both images together with the proportion or intensity of each adjusted through the use of a control of some means and this allows spatial correlation of the input images. For example the two original images might be supplied in overlapping relation to a monitor screen of a PC, and the two images be relatively faded in and faded out in order to change from viewing one image to another.

The display first shows an image, which may or may not be magnified, of the lesion as it actually appears to the eye or a surface microscopy view or an image taken using cross polarised illumination or an image showing a particular feature. By selecting a particular feature such as blood or areas of melanin invasion into the dermis or melanin within the epidermis etc. the display can then be faded to show this feature as an image. The fading allows a progression, or mixing, between the two views and is a convenient means of allowing a spatial correlation to be made between the features and the lesion image.

The images may be images representing the presence of particular existing features of the skin or one or more of them may be computer generated images representing the predicted effects of a treatment such as a laser irradiation treatment. For example, as mentioned above, it is possible to generate a colour representation of the expected result of a laser irradiation treatment, and it would be possible to generate one such image for each of a set of different irradiation intensities. This would enable a comparison of the different courses of treatment and would allow selection of an appropriate treatment, for example the one giving the most cosmetically acceptable result.

The analysis afforded by the present invention is also of value in the selection of the wavelength or wavelengths of any light (infra-red, visible or ultra-violet) irradiation treatment that may be indicated. For example, a knowledge of the constituents of a lesion allows a selection of a wavelength of light radiation which will be most strongly and preferentially absorbed by constituents of that lesion. Also, a knowledge of the existence and structure and composition of overlying tissue (including any discontinuities which it might contain) allows the most favourable compromise to be reached between low absorption in the overlying tissue and high absorption in the lesion to be destroyed, thus providing the most effective treatment with the lowest radiation dosage. Thus a laser of an appropriate wavelength may be selected, and/or a variable wavelength laser may be tuned, or an appropriate filter set may be used in conjunction with a source of non-coherent radiation.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